Dialytic therapy for AKI;

By

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ROAD MAP
5 Ws

1-What are the different modalities ?.

2-When to start ?.

3- What are the best modailty for patients and renal Outcome ?.

4- Which Dose to deliver ?.

5- When to stop?

- **Acute kidney injury is a common complication of acute illness, affecting approximately 2 to 7% of hospitalized patients and more than 35% of critically ill patients.**

- **Renal- replacement therapy is the mainstay of supportive treatment of patients with severe acute kidney injury; its use is required in 5 to 6% of critically ill patients and is associated with in-hospital mortality rates of 50 to 80%.**

- **Of patients who survive an episode of ARF in the ICU, 5% to 30% will remain on long-term dialysis therapy without renal recovery.**

(Barton 1993; Chertow 2015).

Diagnosis and Classification

RIFLE and AKIN Criteria for Diagnosis and Classification of AKI

RIFLE		AKIN	
Class	**SCr[a]**	**Stage**	**SCr[b]**
Risk	Increased SCr to >1.5× baseline	1	Increase in SCr ≥0.3 mg/dL or increase in SCr to ≥150%-200% of baseline
Injury	Increased SCr to >2× baseline	2	Increase in SCr to >200%-300% of baseline
Failure	Increased SCr to >3× baseline; or an increase of ≥0.5 mg/dL to a value of ≥4 mg/dL	3	Increase in SCr to >300% of baseline; or to ≥4 mg/dL with an acute increase of ≥0.5 mg/dL; or on RRT
Loss	Need for RRT for >4 wk		
End Stage	Need for RRT for >3 mo		

Abbreviations: AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; RIFLE, risk, injury, failure, loss, end-stage disease; RRT, renal replacement therapy; SCr, serum creatinine.

[a]For RIFLE, the increase in SCr should be both abrupt (within 1-7 days) and sustained (>24 hours).

[b]For AKIN, the increase in SCr must occur in less than 48 hours.

Goals of Renal Replacement Therapy

- i) To maintain fluid and electrolyte, acid-base, and solute homeostasis
- ii) To permit renal recovery and to prevent further insults to the kidney
- iii) To allow other supportive measures (e.g., antibiotics, nutrition support) to proceed without limitation or complication.

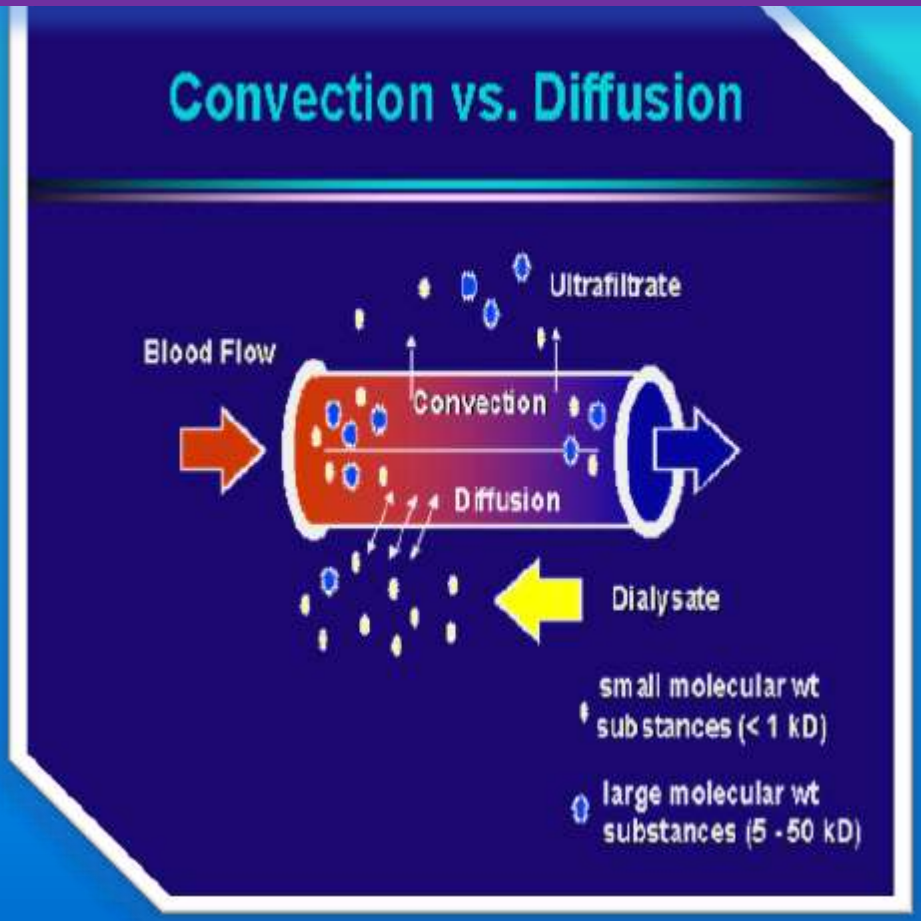
Kidney Disease: Improving Global Outcomes (KDIGO), 2012

1St W
Which Modality?

Which Modality?

1. **Intermittent Hemodialysis (IHD)**
2. **Slow Low-Efficiency Daily Dialysis (SLED)**
3. **Peritoneal dialysis (PD)**
4. **Continuous Renal Replacement Therapy (CRRT)**
   - **Slow Continuous Ultrafiltration (SCUF)**
   - **Continuous Venovenous Hemofiltration (CVVH)**
   - **Continuous Venovenous Hemodialysis (CVVHD)**
   - **Continuous Venovenous Hemodiafiltration (CVVHDF)**

Which Modality?
Back to the basics



Mode of therapy	*Principle method of solute clearance*
CVVH	
CVVHD	
CVVHDF	
SCUF	

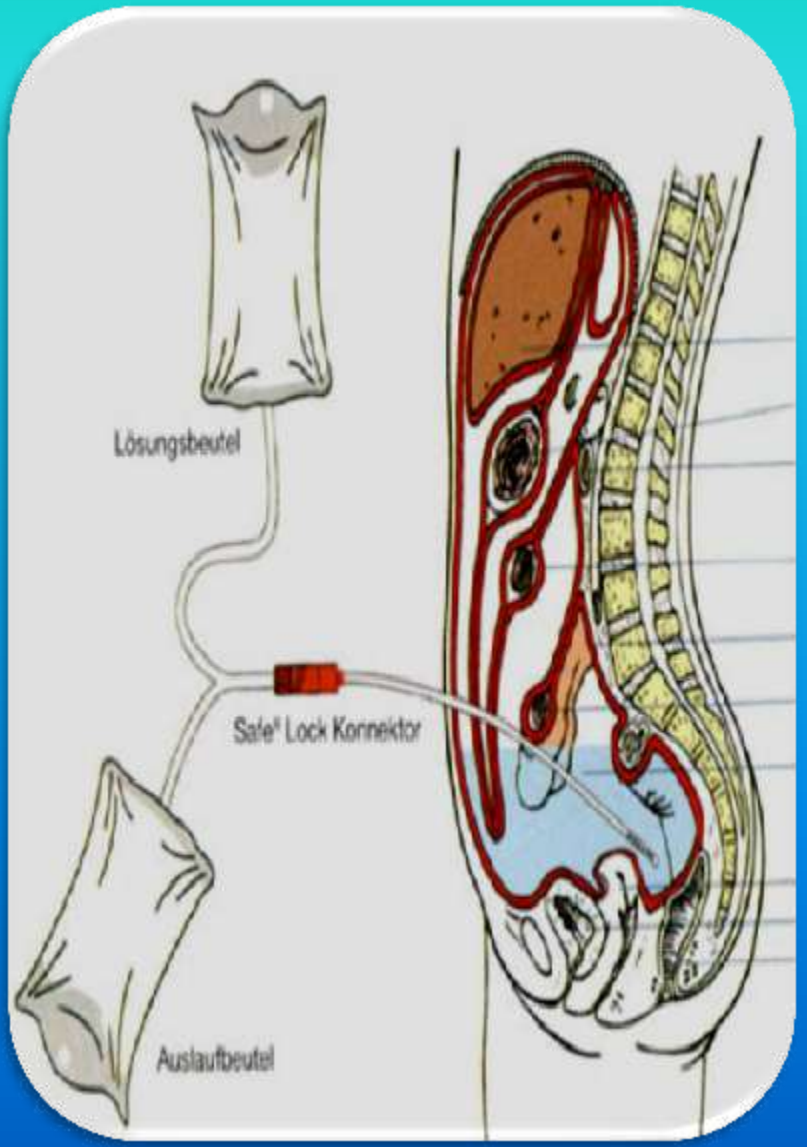
Which Modality?

Advantages

- Cardiovascular stability
- *Slow correction*
- *Easy access placement*
- *No Anticoagulation*
- *Tolerated in children*
- Low bleeding risk
- The absence of an extracorporeal circuit.

Disadvantages

- Risk of infections
- Difficulty to use with abdominals surgery.



Which Modality?

Modality	Potential setting in AKI	Advantages	Disadvantages
IHD	Hemodynamically stable	Rapid removal of toxins and low-molecular-weight substances Allows for "down time" for diagnostic and therapeutic procedures Reduced exposure to anticoagulation Lower costs than CRRT	Hypotension with rapid fluid removal Dialysis disequilibrium with risk of cerebral edema Technically more complex and demanding
CRRT	Hemodynamically unstable Patients at risk of increased intracranial pressure	Continuous removal of toxins Hemodynamic stability Easy control of fluid balance No treatment-induced increase of intracranial pressure User-friendly machines	Slower clearance of toxins Need for prolonged anticoagulation Patient immobilization Hypothermia Increased costs
SLED	Hemodynamically unstable	Slower volume and solute removal Hemodynamic stability Allows for "down time" for diagnostic and therapeutic procedures Reduced exposure to anticoagulation	Slower clearance of toxins Technically more complex and demanding

Which Modality?

- ***5.6.2:*** We suggest using **CRRT, rather than standard intermittent RRT,** for **hemodynamically unstable patients**. **(2B)**

- ***5.6.1***: Use **continuous and intermittent RRT as complementary therapies** in AKI patients. **(Not Graded**

KDIGO® AKI Guideline March 2012

2nd W
When to start ?

When to start ?

- ***5.1.1***: ***Initiate RRT emergently*** when **life-threatening** changes in fluid, electrolyte, and acid-base balance exist.(Not Graded)
- ***5.1.2***: ***trends of laboratory*** tests—rather than single BUN and creatinine thresholds alone—when making the decision to start RRT. (Not Graded)

KDIGO® AKI Guideline March 2012

When to start ?

Renal Indications

Life-threatening indications

- ***Hyperkalemia***
- ***Metabolic Acidosis***
- ***Pulmonary edema***
- ***Uremic Complications***

Indication	Characteristics	Absolute/Relative
Metabolic abnormality	BUN > 76 mg/dl (27 mmol/L)	Relative
	BUN > 100 mg/dl (35.7 mmol/L)	Absolute
	Hyperkalemia > 6 mEq/L	Relative
	Hyperkalemia > 6 mEq/L with ECG abnormalities	Absolute
	Dysnatremia	Relative
	Hypermagnesemia > 8 mEq/L (4 mmol/L)	Relative
	Hypermagnesemia > 8 mEq/L (4 mmol/L) with anuria and absent deep tendon reflexes	Absolute
Acidosis	pH > 7.15	Relative
	pH < 7.15	Absolute
	Lactic acidosis related to metformin use	Absolute
Anuria/oliguria	RIFLE class R	Relative
	RIFLE class I	Relative
	RIFLE class F	Relative
Fluid overload	Diuretic sensitive	Relative
	Diuretic resistant	Absolute

Gibney et al, Clin J Am Soc Nephrol 2008

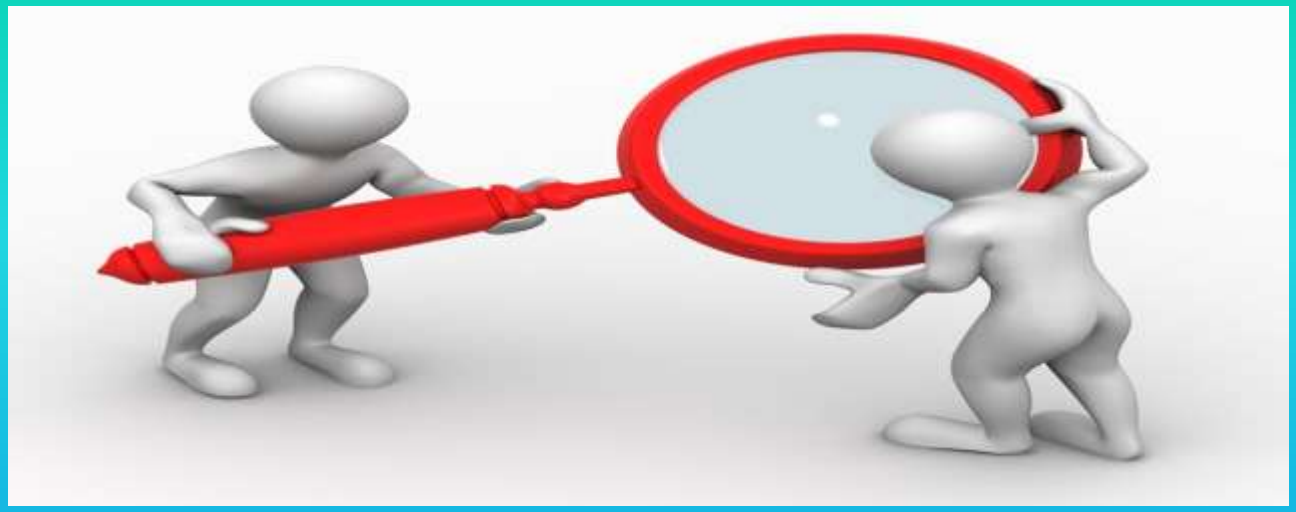
When to start ?

Benefits

- Avoiding hypervolemia .
- Eliminating of toxins .
- Establishing acid-base homeostasis.
- Preventing other complications attributable to AKI.
- Attenuate kidney-specific and non–kidney organ injury from acidemia, uremia, fluid overload, and systemic inflammation .
- Could potentially translate into improved survival and earlier recovery of kidney function

Disadvantage

- Early initiation of RRT may unnecessarily expose some patients to potential harm because some patients will spontaneously recover renal function.
- Risk Of Anticoagulation
- Risk Of CRB
- Risk of hypophosphatemia




EVIDENCE
EVIDENCE

When to start ?

Crit Care Med 2008 Vol. 36, No. 4 (Suppl.)

Indications and timing of renal replacement therapy in acute kidney injury

Paul M. Palevsky, MD

The optimal timing for initiation of renal replacement therapy in patients with acute kidney injury remains uncertain. Conventionally accepted indications include volume overload, hyperkalemia, metabolic acidosis, overt uremia, and even progressive azotemia in the absence of specific symptoms; however, precise definitions for these indications are lacking. Data from recent observational trials have suggested that early initiation of renal replacement therapy may be associated with decreased mortality; however, the results of these studies are inconclusive. Existing data on timing of initiation of renal replacement therapy in acute kidney injury that guide current clinical practice are summarized and issues that need to be addressed in future clinical trials are discussed. (Crit Care Med 2008; 36[Suppl.]:S224–S228)

KEY WORDS: renal replacement therapy; acute kidney injury; volume overload; hyperkalemia; metabolic acidosis

10 …up

One st… group

Early RRT seems better

When to start ?

Preexisting Chronic Kidney Disease: A Potential for Improved Outcomes from Acute Kidney Injury

Nitin Khosla,* Sharon B. Soroko,* Glenn M. Chertow,† Jonathan Himmelfarb,‡ T. Alp Ikizler,§ Emil Paganini,‖ and Ravindra L. Mehta,* for the Program to Improve Care in Acute Renal Disease (PICARD)

*University of California San Diego, San Diego, California; †Division of Nephrology, Stanford University School of Medicine, Palo Alto, California; ‡Kidney Research Institute, University of Washington, Seattle, Washington; §Vanderbilt University Medical Center, Nashville, Tennessee; ‖Cleveland Clinic Foundation, Cleveland, Ohio

Clin J Am Soc Nephrol 4: 1914–1919, 2009.

When to start ?

Karvellas *et al. Critical Care* 2011, **15**:R72
http://ccforum.com/content/15/1/R72

CRITICAL CARE

RESEARCH Open Access

A comparison of early versus late initiation of renal replacement therapy in critically ill patients with acute kidney injury: a systematic review and meta-analysis

Constantine J Karvellas[1], Maha R Farhat[2], Imran Sajjad[3], Simon S Mogensen[4], Alexander A Leung[5], Ron Wald[6], Sean M Bagshaw[1*]

When to start ?

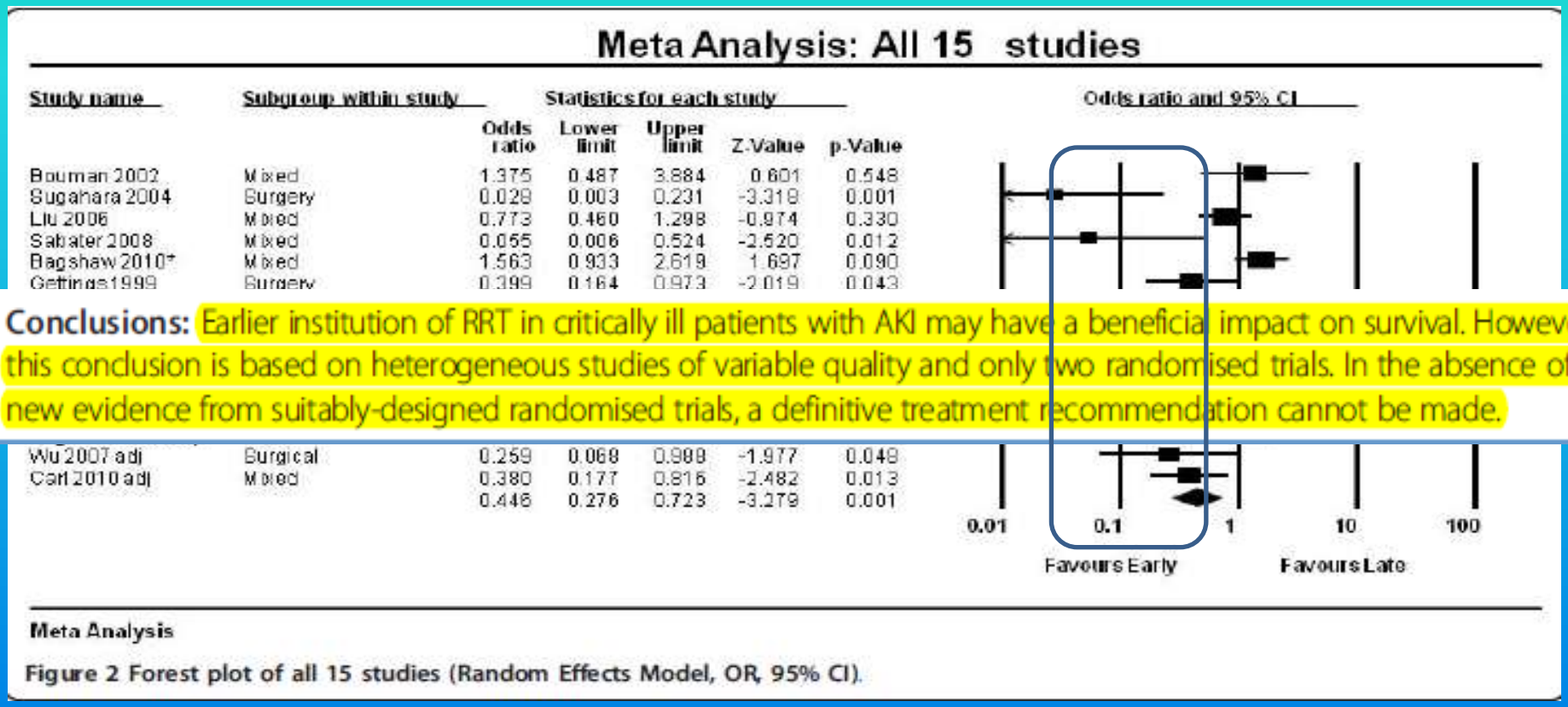


Figure 2 Forest plot of all 15 studies (Random Effects Model, OR, 95% CI).

Conclusions: Earlier institution of RRT in critically ill patients with AKI may have a beneficial impact on survival. However, this conclusion is based on heterogeneous studies of variable quality and only two randomised trials. In the absence of new evidence from suitably-designed randomised trials, a definitive treatment recommendation cannot be made.

Early RRT initiation was associated with reduced mortality compared to late initiation ($P < 0.001$).

When to start ?

Research

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of Early vs Delayed Initiation of Renal Replacement Therapy on Mortality in Critically Ill Patients With Acute Kidney Injury

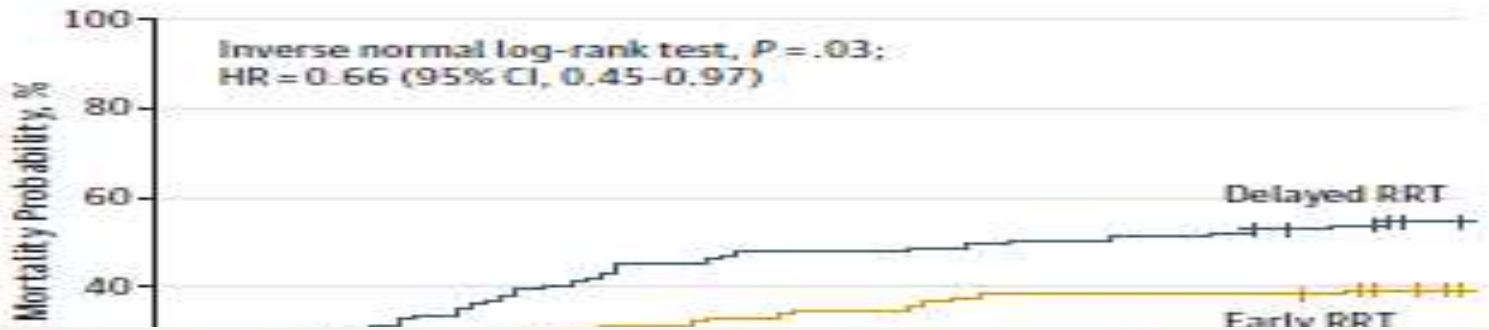
The ELAIN Randomized Clinical Trial

Alexander Zarbock, MD; John A. Kellum, MD; Christoph Schmidt, MD; Hugo Van Aken, MD; Carola Wempe, PhD; Hermann Pavenstädt, MD; Andreea Boanta, MD; Joachim Gerß, PhD; Melanie Meersch, MD

JAMA Published online May 22, 2016

When to start ?

for Patients Receiving Early and Delayed Initiation of Renal Replacement Therapy (RRT)



CONCLUSIONS AND RELEVANCE Among critically ill patients with AKI, early RRT compared with delayed initiation of RRT reduced mortality over the first 90 days. Further multicenter trials of this intervention are warranted.

KDIGO indicates Kidney Disease: Improving Global Outcomes. In the delayed group, 18 patients received RRT without reaching KDIGO stage 3 (these patients had an absolute indication). The median (quartile 1 [Q1], quartile 3 [Q3]) duration of follow-up was 90 days (Q1, Q3: 90, 90) in the early group and 90 days (Q1, Q3: 90, 90) in the delayed group. The vertical ticks indicate censored cases.

Early initiation of RRT significantly reduced 90-day mortality compared with delayed initiation of RRT .

Conclusion

Indications and timing of renal replacement therapy in acute kidney injury

Paul M. Palevsky, MD

The optimal timing for initiation of renal replacement therapy in patients with acute kidney injury remains uncertain. Conventionally accepted indications include volume overload, hyperkalemia, metabolic acidosis, overt uremia, and even progressive azotemia in the absence of specific symptoms; however, precise definitions for these indications are lacking. Data from recent observational trials have suggested that early initiation of renal replacement therapy may be associated with decreased mortality; however, the results of these studies are inconclusive. Existing data on timing of initiation of renal replacement therapy in acute kidney injury that guide current clinical practice are summarized and issues that need to be addressed in future clinical trials are discussed. (Crit Care Med 2008; 36[Suppl.]:S224–S228)

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Karvellas et al. Critical Care 2011, 15:R72
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Preexisting Chronic Kidney Disease: A Potential for Improved Outcomes from Acute Kidney Injury

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Do outcomes matter?

3rd W
Modality and Pateint,s outcome

Randomized trials comparing CRRT with IHD in ICU

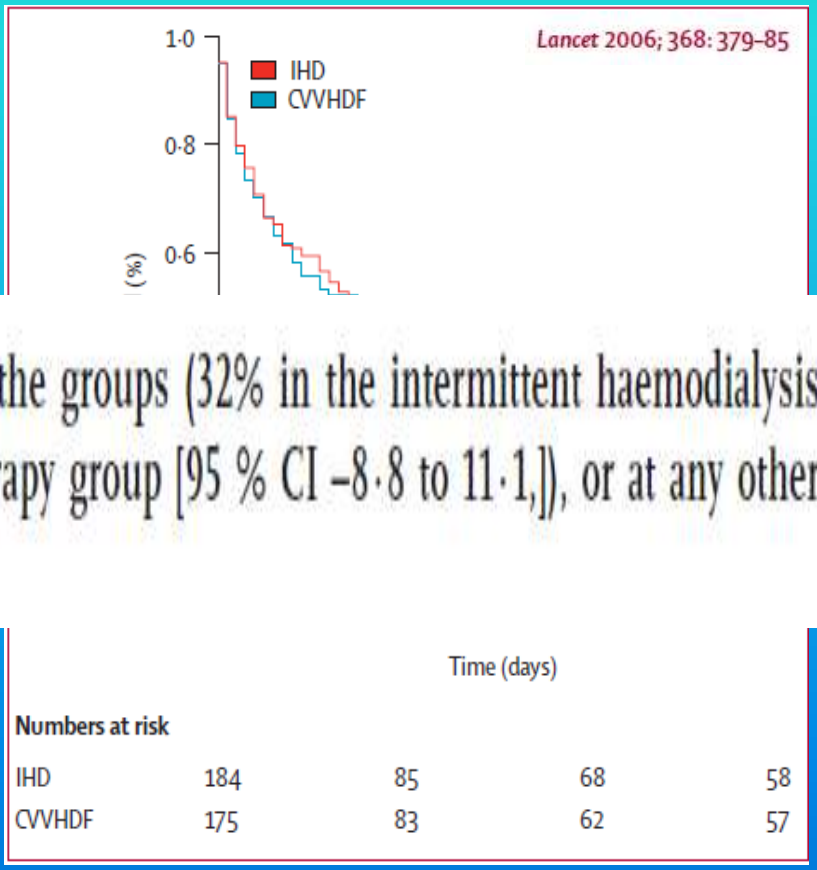
Study	Type	*n*	Comparison	Mortality*
Lins *et al.* (2009)[30]	Multicenter RCT	316	CVVHF vs IHD	58% vs 63% (*P*=ns)
Vinsonneau *et al.* (2006)[29]	Multicenter RCT	359	CVVHDF vs IHD	32% vs 33% a day 60 (*P*=ns
Uehlinger *et al.* (2005)[28]	Single-center RCT	125	CVVHDF vs IHD	47% vs 51% (*P*=ns)
Augustine *et al.* (2004)[27]	Single-center RCT	80	CVVHD vs IHD	68% vs 70% (*P*=ns)
Kielstein *et al.* (2004)[26]	Single-center RCT	39	CVVHF vs extended daily dialysis	40% vs 40% (*P*=ns)
Mehta *et al.* (2001)[24]	Multicenter RCT	166	CVVHDF vs IHD	66% vs 48% (*P*=0.02)
John *et al.* (2001)[25]	Single-center RCT	30	CVVHF vs IHD	70% vs 70% (*P*=ns)

Prowle, J. R. & Bellomo, R. (2010) *Nat. Rev. Nephrol.* 2010.100

Continuous venovenous haemodiafiltration versus intermittent haemodialysis for acute renal failure in patients with multiple-organ dysfunction syndrome: a multicentre randomised trial

Christophe Vinsonneau, Christophe Camus, Alain Combes, Marie Alyette Costa de Beauregard, Kada Klouche, Thierry Boulain, Jean-Louis Pallot, Jean-Daniel Chiche, Pierre Taupin, Paul Landais, Jean-François Dhainaut, for the Hemodiafe Study Group*

- From Oct 1, 1999, to March 3, 2003, we did a prospective randomised, non-blinded trial in 21



Findings Rate of survival at 60-days did not differ between the groups (32% in the intermittent haemodialysis group versus 33% in the continuous renal replacement therapy group [95 % CI −8·8 to 11·1,]), or at any other time.

randomised, and the primary endpoint was 60-day survival based on an intention-to-treat analysis.

REVIEW

Renal Replacement Therapy in Patients With Acute Renal Failure

A Systematic Review

Neesh Pannu, MD, SM
Scott Klarenbach, MD, MSc
Natasha Wiebe, MMath, PStat
Braden Manns, MD, MSc
Marcello Tonelli, MD, SM
for the Alberta Kidney Disease Network

- **ttent Hemodialysis:**
- tal participants) that compared

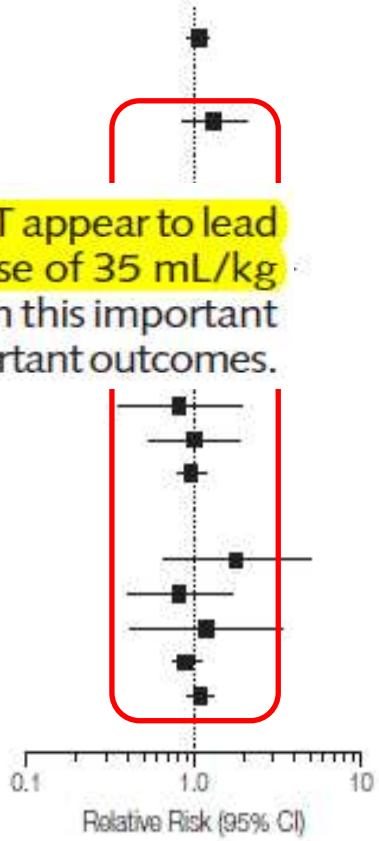
(Reprinted) JAMA, February 20, 2008—Vol 299, No. 7 793

Renal Replacement Therapy in Patients With Acute Renal Failure

A Systematic Review

Comparison	References	Mortality, No./Total No. Group 1	Group 2	Relative Risk (95% CI)
Continuous renal replacement therapy vs intermittent hemodialysis	17, 19, 20, 23, 25, 28, 29	293/469	254/449	1.10 (0.99-1.23)
Continuous renal replacement therapy vs sustained low-efficiency dialysis	23	20/28	14/26	1.33 (0.87-2.03)
C				
Hirudin vs heparin	21	5/12	7/14	0.83 (0.36-1.95)
P2SH vs polyamide[b]	15	11/18	6/10	1.02 (0.54-1.90)
Polyacrylonitril vs polysulfone	39	69/97	73/100	0.97 (0.82-1.16)
Intermittent hemodialysis				
Hemodiafiltration vs hemodialysis	30	9/21	4/17	1.82 (0.68-4.90)
Daily vs alternate days	27, 44	32/97	45/97	0.83 (0.40-1.72)
Acetate-free vs bicarbonate	37	6/16	4/13	1.22 (0.43-3.42)
High vs low membrane flux	31, 34, 40, 42	76/138	91/149	0.91 (0.74-1.11)
Bioincompatible membrane vs biocompatible membrane	32, 34, 36, 38, 40-42	161/336	173/383	1.11 (0.94-1.31)

Conclusions Based on current data, intermittent hemodialysis and CRRT appear to lead to similar clinical outcomes for patients with ARF. If CVVHF is used, a dose of 35 mL/kg per hour should be provided. Given the paucity of good-quality evidence in this important area, additional large randomized trials are needed to evaluate clinically important outcomes.



Schefold et al. Critical Care 2014, 18:R11
http://ccforum.com/content/18/1/R11

CRITICAL CARE

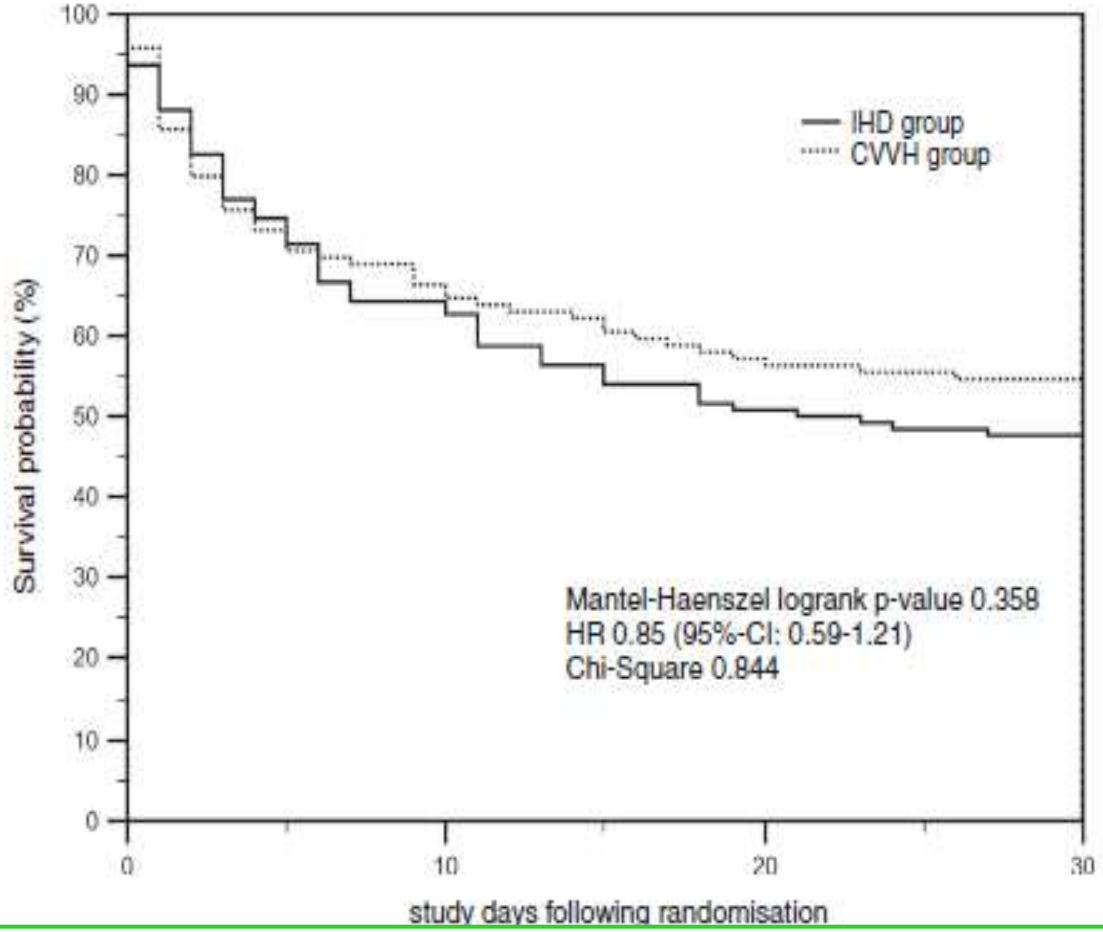
RESEARCH Open Access

The effect of continuous versus intermittent renal replacement therapy on the outcome of critically ill patients with acute renal failure (CONVINT): a prospective randomized controlled trial

CONtinuous **Vs. INT**ermittent RRT on the outcome of critically ill patients with ARF trial

(CONVINT)

CONtinuous Vs. INTermittent RRT on the outcome of critically ill patients with ARF trial (CONVINT)



- No statistically significant differences regarding 14-day-, 30-day-, all cause intrahospital mortality, renal-related outcome measures, or survival at 14 days after RRT.

Conclusion

What are the best modailty for patients Outcome ?.

Continuous venovenous haemodiafiltration versus intermittent haemodialysis for acute renal failure in patients with multiple-organ dysfunction syndrome: a multicentre randomised trial

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REVIEW

Renal Replacement Therapy in Patients With Acute Renal Failure

A Systematic Review

http://ccforum.com/content/18/1/R11

CRITICAL CARE

RESEARCH Open Access

The effect of continuous versus intermittent renal replacement therapy on the outcome of critically ill patients with acute renal failure (CONVINT): a prospective randomized controlled trial


4th W; What are the best modailty for renal Outcome?
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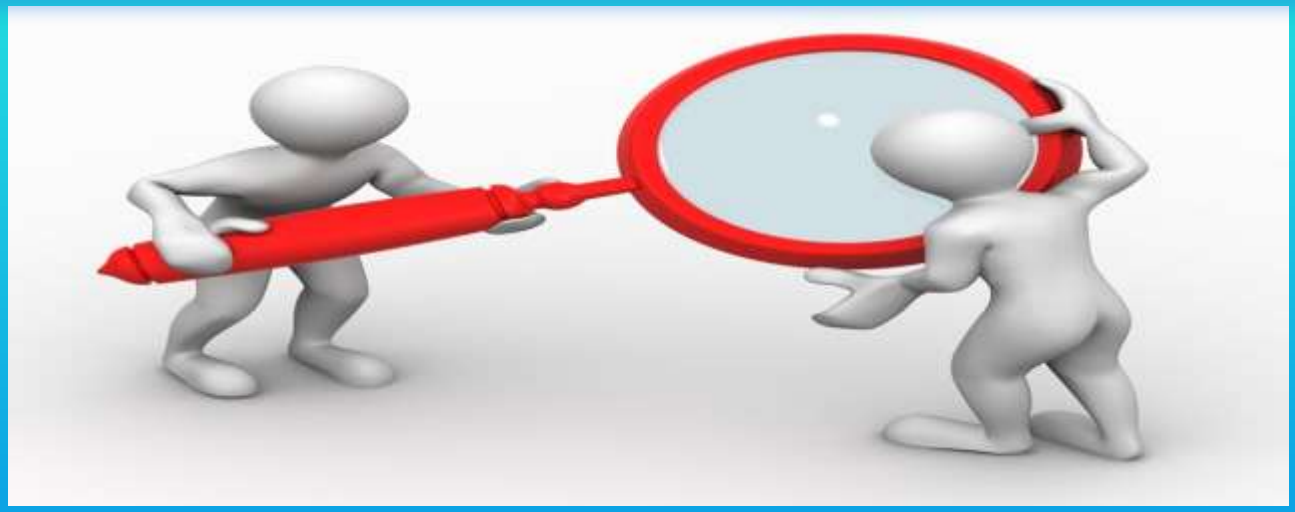
What are the best Modality for renal Outcome?

- **In theory, because of its rapid changes in fluid status and plasma osmolality, IRRT induces a decrease in venous return and cardiac index. Because of this effect, IRRT may cause renal ischemia and delay renal recovery after AKI.**

- **Therefore, if IRRT causes intradialytic hypotension more frequently than CRRT, it is likely that IRRT can prolong renal recovery.**

What are the best modailty renal Outcome?



The International Journal of Artificial Organs / Vol. 30 / no. 4, 2007 / pp. 281-292

Patient and kidney survival by dialysis modality in critically ill patients with acute kidney injury

S. UCHINO[1], R. BELLOMO[2], J. A. KELLUM[3], H. MORIMATSU[2], S. MORGERA[4], M. SCHETZ[5], I.TAN[6], C. BOUMAN[7], E. MACEDO[8], N. GIBNEY[9], A. TOLWANI[10], H. OUDEMANS-VAN STRAATEN[11], C. RONCO[12]

Beginning and Ending Supportive Therapy for the Kidney (B.E.S.T. Kidney) Investigators Writing Committee

The International Journal of Artificial Organs / Vol. 30 / no. 4, 2007 / pp. 281-292

Artificial Kidney and Dialysis

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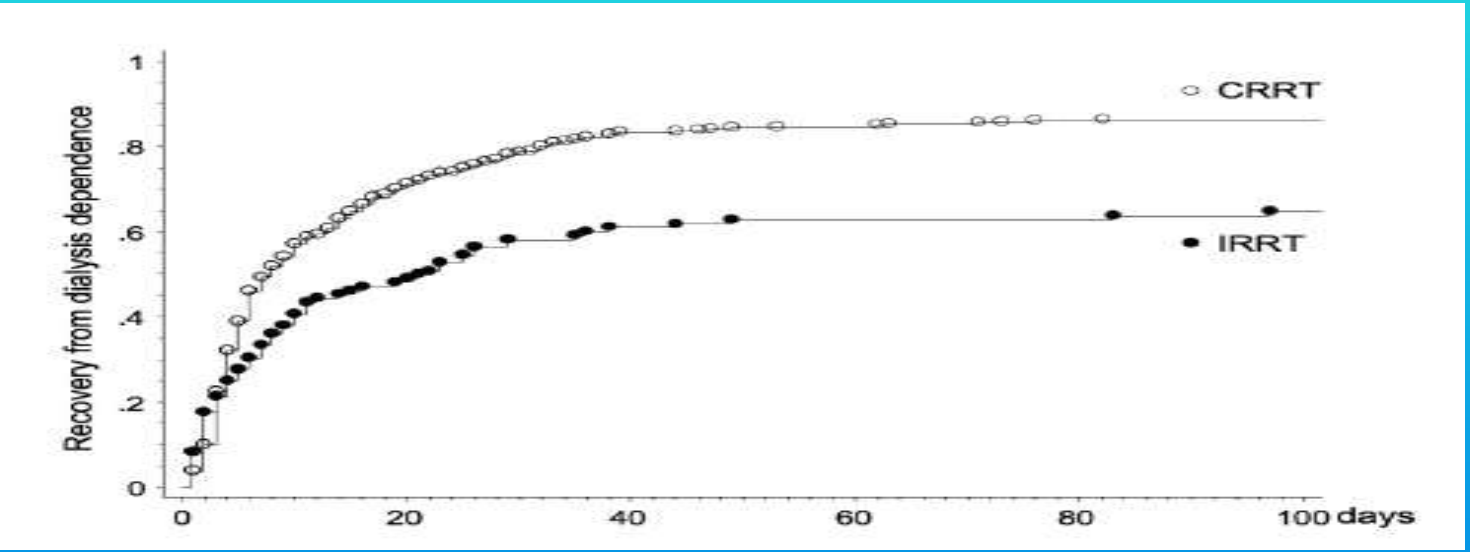

results. We conclude that worldwide, the choice of CRRT as initial therapy is not a predictor of hospital survival or dialysis-free hospital survival but is an independent predictor of renal recovery among survivors. (Int J Artif Organs 2007; 30: 281-92)

What are the best modailty for patients and renal Outcome?

Choice of therapy and renal recovery

Shigehiko Uchino, MD

Objectives: To describe the impact of choice of therapy on renal recovery.

Design: Literature review.

Main Results: Randomized controlled trials conducted have not shown a benefit of continuous renal replacement therapy in mortality over intermittent renal replacement therapy. However, renal recovery is another important outcome for patients with acute kidney injury and may be affected differently by intermittent renal replacement therapy and continuous renal replacement therapy. Because of its rapid changes in fluid status and plasma osmolality, intermittent renal replacement therapy induces a decrease in venous return and can induce intradialytic hypotension. Because of this effect, intermittent renal replacement therapy may cause renal ischemia and delay renal recovery. Observational studies, including two large epidemiologic studies, suggest that continuous renal replacement therapy may be able to reduce chronic dialysis dependence. On the other hand, randomized controlled trials conducted so far do not support an effect of continuous renal replacement therapy over intermittent renal replacement therapy in relation to renal recovery. However, all of these randomized studies have significant limitations including sample size, study design, and randomization.

Conclusions: Although there is much suggestive evidence that continuous renal replacement therapy may increase the rate of renal recovery, such evidence is insufficient to fully elucidate the impact of choice of therapy on this outcome. Appropriately planned trials will be required to address this issue. (Crit Care Med 2008; 36[Suppl.]:S238–S242)

KEY WORDS: acute renal failure; epidemiology; continuous renal replacement therapy; intermittent renal replacement therapy; critical illness; hemodialysis; hemofiltration; end-stage kidney disease; renal function; intensive care unit

Choice of therapy and renal recovery

Shigehiko Uchino, MD

Table 1. Observational studies of renal replacement therapy (RRT) for acute renal failure reporting renal recovery

First Author	Published Year	Reference	No. of Patients	Treated with CRRT (%)	Survived	Dialysis Dependence (%)
Barton	1993	19	250	250 (100)	132	4 (3.0)
Consentino	1994	20	363	194 (53.4)	76	26 (34.2)
Chertow[a]	1995	21	132	52 (39.4)	39	13 (33.3)
Swartz	1999	22	349	166 (47.5)	143	52 (36.4)
Cole	2000	23	116	110 (94.8)	59	11 (18.6)
Korkeila	2000	24	62	46 (74.2)	34	11 (32.4)
Silvester	2001	25	299	292 (97.7)	159	25 (15.7)
Manns	2003	9	261	178 (68.2)	98	28 (28.6)
Bell	2005	26	207	207 (100)	105	5 (4.8)
Ahlstrom	2005	27	703	207 (29.4)	294	37 (12.6)
Bagshaw[a]	2005	28	240	192 (80.0)	87	19 (21.8)
Jacka	2005	29	93	65 (69.9)	38	12 (31.6)
Maccariello	2007	30	214	178 (83.2)	52	10 (19.2)

[a]1-yr outcomes. Dialysis dependence is rate of patients who remained on dialysis at hospital discharge among survivors.

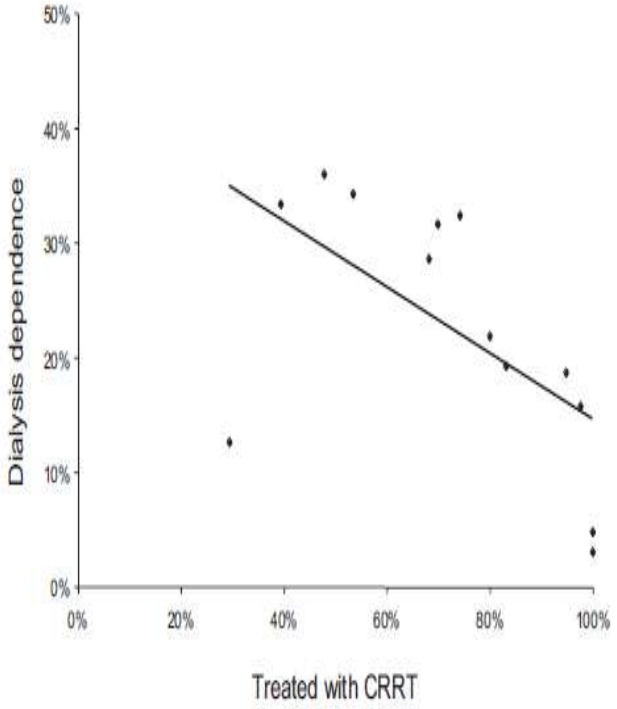

Figure 1. Relationship between the use of continuous renal replacement therapy (*CRRT*) and the prevalence of dialysis dependence among survivors.

13 Observational studies consistently support the notion that IRRT may delay renal recovery.

The more patients that are treated with CRRT, the lower the rate of dialysis dependence is.

What are the best modailty for patients and renal Outcome?

Intensive Care Med (2013) 39:987–997
DOI 10.1007/s00134-013-2864-5

SYSTEMATIC REVIEW

Antoine G. Schneider
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Choice of renal replacement therapy modality and dialysis dependence after acute kidney injury: a systematic review and meta-analysis

The primary outcome was dialysis dependence among survivors.

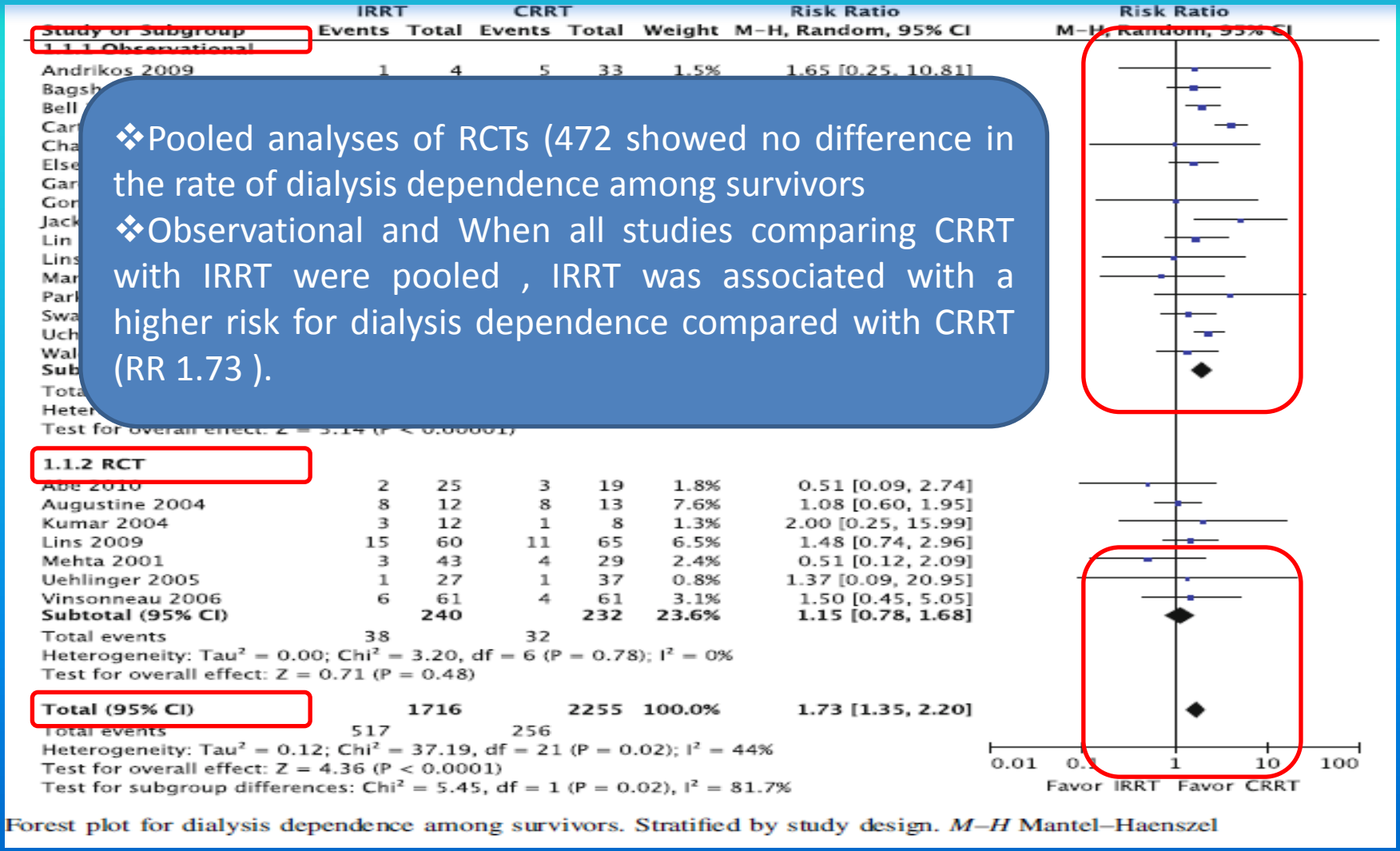
What are the best modailty for patients and renal Outcome?

- all RCTs and observational studies in English language reporting data on dialysis dependence after RRT for AKI between 2000 and 2012.
- 23 studies: 17 observational and 6 RCT

What are the best modailty for patients and renal Outcome?

❖Pooled analyses of RCTs (472 showed no difference in the rate of dialysis dependence among survivors

❖Observational and When all studies comparing CRRT with IRRT were pooled , IRRT was associated with a higher risk for dialysis dependence compared with CRRT (RR 1.73).



Forest plot for dialysis dependence among survivors. Stratified by study design. *M–H* Mantel–Haenszel

Conclusion

What are the best modailty for renal Outcome?

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Artificial Kidney and Dialysis

Patient and kidney survival by dialysis modality in critically ill patients with acute kidney injury

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Beginning and Ending Supportive Therapy for the Kidney (B.E.S.T. Kidney) Investigators Writing Committee

Choice of therapy and renal recovery

Shigehiko Uchino, MD

Objectives: To describe the impact of choice of therapy on renal recovery.

Design: Literature review.

Main Results: Randomized controlled trials conducted have not shown a benefit of continuous renal replacement therapy in mortality over intermittent renal replacement therapy. However, renal recovery is another important outcome for patients with acute kidney injury and may be affected differently by intermittent renal replacement therapy and continuous renal replacement therapy. Because of its rapid changes in fluid status and plasma osmolality, intermittent renal replacement therapy induces a decrease in venous return and can induce intradialytic hypotension. Because of this effect, intermittent renal replacement therapy may cause renal ischemia and delay renal recovery. Observational studies, including two large epidemiologic studies, suggest that continuous renal replacement therapy may be able to reduce chronic dialysis dependence. On the other hand, randomized controlled trials conducted so far do not support an effect of continuous renal replacement therapy over intermittent renal replacement therapy in relation to renal recovery. However, all of these randomized studies have significant limitations including sample size, study design, and randomization.

Conclusions: Although there is much suggestive evidence that continuous renal replacement therapy may increase the rate of renal recovery, such evidence is insufficient to fully elucidate the impact of choice of therapy on this outcome. Appropriately planned trials will be required to address this issue. (Crit Care Med 2008; 36[Suppl.]:S238–S242)

KEY WORDS: acute renal failure; epidemiology; continuous renal replacement therapy; intermittent renal replacement therapy; critical illness; hemodialysis; hemofiltration; end-stage kidney disease; renal function; intensive care unit

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4- Which Dose to deliver ?

4- Dose and outcome

REVIEWS

Fluid balance and acute kidney injury

John R. Prowle, Jorge E. Echeverri, E. Valentina Ligabo, Claudio Ronco and Rinaldo Bellomo

FEBRUARY 2010 | VOLUME 6 www.nature.com/nrneph

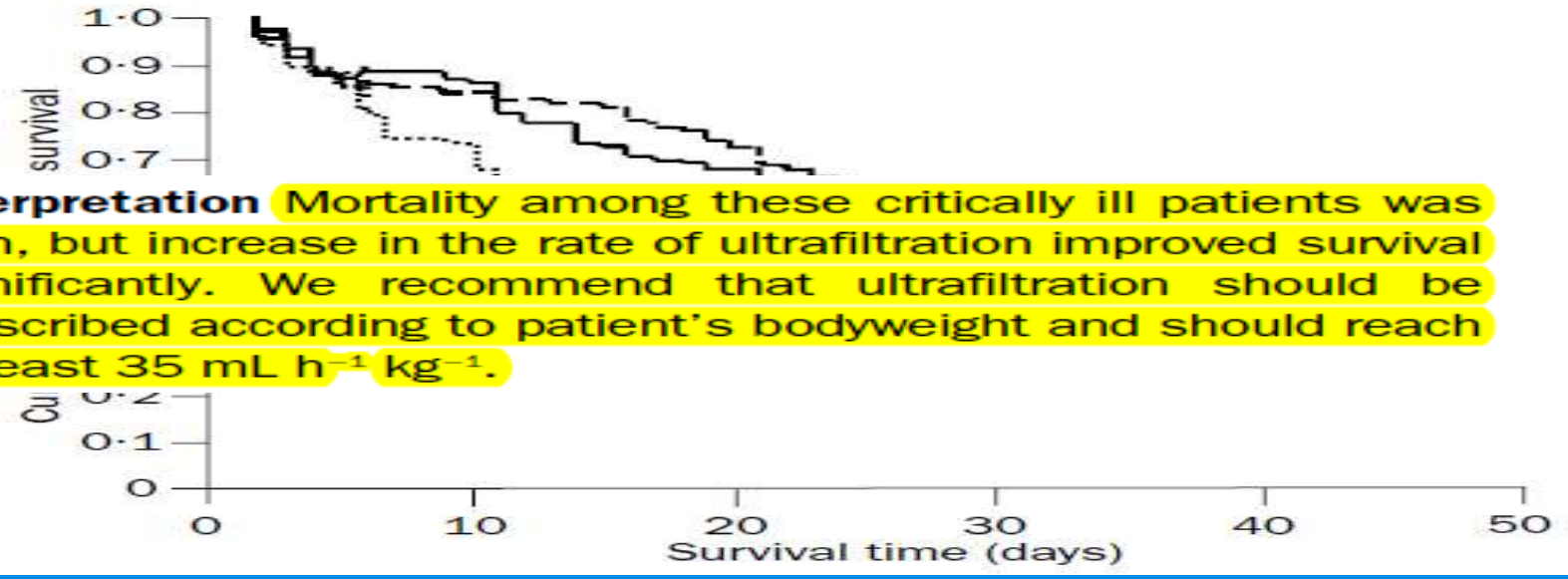
Study	Type	*n*	Comparison	Mortality	Mortality end point	Comment
RENAL (2009)[18]	Multicenter RCT	1,508	40 ml/kg per h vs 25 ml/kg per h post-dilution CVVHDF	45% vs 45% (*P*=ns)	Day 90	—
ATN (2008)[17]	Multicenter RCT	1,124	Pre-dilution CVVHDF 35 ml/kg per h or SLEDD 6 times weekly or IHD 6 times weekly vs pre-dilution CVVHDF 20 ml/kg per h or SLEDD 3 times weekly or IHD 3 times weekly	54% vs 52% (*P*=ns)	Day 60	Choice of CRRT/SLEDD vs IHD based on daily cardiovascular SOFA score
Tolwani *et al.* (2008)[58]	Single-center RCT	200	Pre-dilution CVVHDF 20 ml/kg per h vs 35 ml/kg per h	56% vs 49% (*P*=ns)	ICU discharge or day 30	—
Saudan *et al.* (2006)[57]	Single-center RCT	204	CVVHF (1–2.5 l/h) vs CVVHDF (1–2.5 l/h HF+1–1.5 l/h HD)	59% vs 39% (*P*=0.0005)	Day 28	Addition of HD to HF (as HDF) vs HF alone
Bouman *et al.* (2002)[53]	Two-center RCT	106	CVVHF 72–96 l per day early vs 24–36 l per day early vs 24–36 l per day late	26% vs 31% (*P*=ns) vs 25% (*P*=ns)	Day 30	Combined trial of dose and timing (early vs late)
Ronco *et al.* (2000)[56]	Single-center RCT	425	Post-dilution CVVHF 20 ml/kg per h vs 35 ml/kg per h vs 45 ml/kg per h	41% vs 57% vs 58% (*P*<0.002 for 20 ml/kg per h vs 35 ml/kg per h and 45 ml/kg per h and *P*=ns for 35 ml/kg per h vs 45 ml/kg per h)	Day 15	Unorthodox mortality outcome (day 15 post-CRRT)

Only prospective randomized controlled trials published in peer-reviewed journals in English are included. Abbreviations: CRRT, continuous renal replacement therapy; CVVHDF, continuous venovenous hemodiafiltration; CVVHF, continuous venovenous hemofiltration; HD, hemodialysis; HDF, hemodiafiltration; HF, hemofiltration; IHD, intermittent hemodialysis; ns, nonsignificant (*P*>0.05); RCT, randomized controlled trial; SLEDD, slow extended-duration dialysis; SOFA, sequential organ failure assessment.

Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomised trial

Claudio Ronco, Rinaldo Bellomo, Peter Homel, Alessandra Brendolan, Maurizio Dan, Pasqu

Lancet 2000; **355:** 26–30



Interpretation Mortality among these critically ill patients was high, but increase in the rate of ultrafiltration improved survival significantly. We recommend that ultrafiltration should be prescribed according to patient's bodyweight and should reach at least 35 mL h^{-1} kg^{-1}.

Survival in group 1 was significantly lower than in groups 2 (p=0·0007) and 3 (p=0·0013). Survival in groups 2 and 3 did not differ significantly (p=0·87).

4- Dose and outcome

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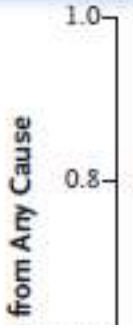
Intensity of Renal Support in Critically Ill Patients with Acute Kidney Injury

The VA/NIH Acute Renal Failure Trial Network*

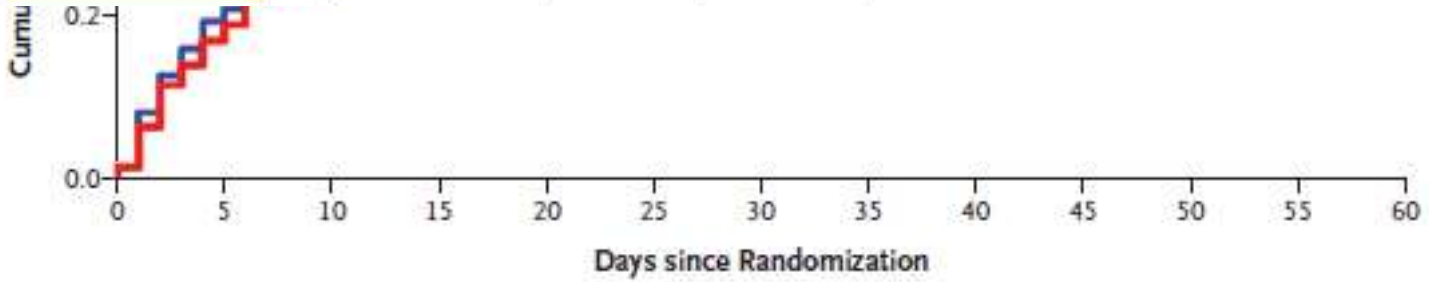
VA/NIH Acute Renal Failure Trial Network. (NEJM 2008;359:7):

4- Dose and outcome



CONCLUSIONS

Intensive renal support in critically ill patients with acute kidney injury did not decrease mortality, improve recovery of kidney function, or reduce the rate of nonrenal



No difference in mortality

VA/NIH Acute Renal Failure Trial Network. (NEJM 2008;359:7):

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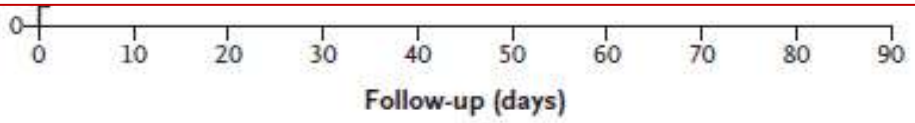
Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients

The RENAL Replacement Therapy Study Investigators*

The Randomized Evaluation of Normal versus Augmented Level (RENAL)



treatment groups.

N Engl J Med. 2009 Oct 22;361(17):1627-38

Conclusion 4

Which Dose to deliver ?

Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomised trial

Claudio Ronco, Rinaldo Bellomo, Peter Homel, Alessandra Brendolan, Maurizio Dan, Pasquale Piccinni, Giuseppe La Greca

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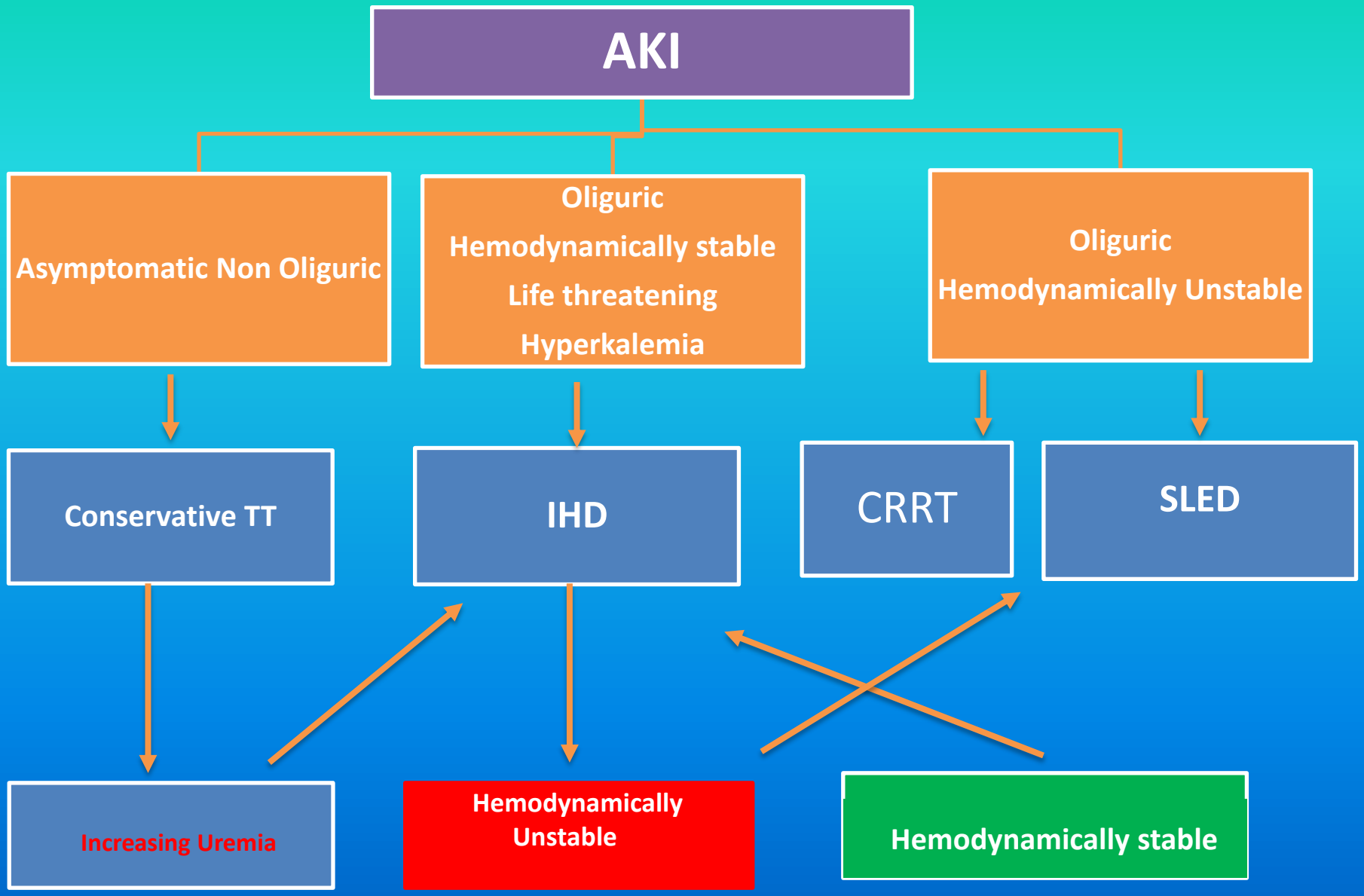
The RENAL Replacement Therapy Study Investigators*

5th W When to Stop?

- **RRT can be stopped when there is sufficient improvement in renal function.**
- **Decisions to delay or stop the next RRT session may be easier for intermittent treatments.**
- **How this can be evaluated while the patient is still receiving RRT remains unclear.**
- **(ATN) study , creatinine clearance was assessed (using a 6-hour urine collection) when urine output exceeded 30 mL/hour or a decrease in creatinine level occurred while on CRRT.**
- **Renal support discontinued when the measured creatinine clearance exceeded 20 mL/minute .**

Algorithm for the dialytic treatment of AKIaccording to circumstances



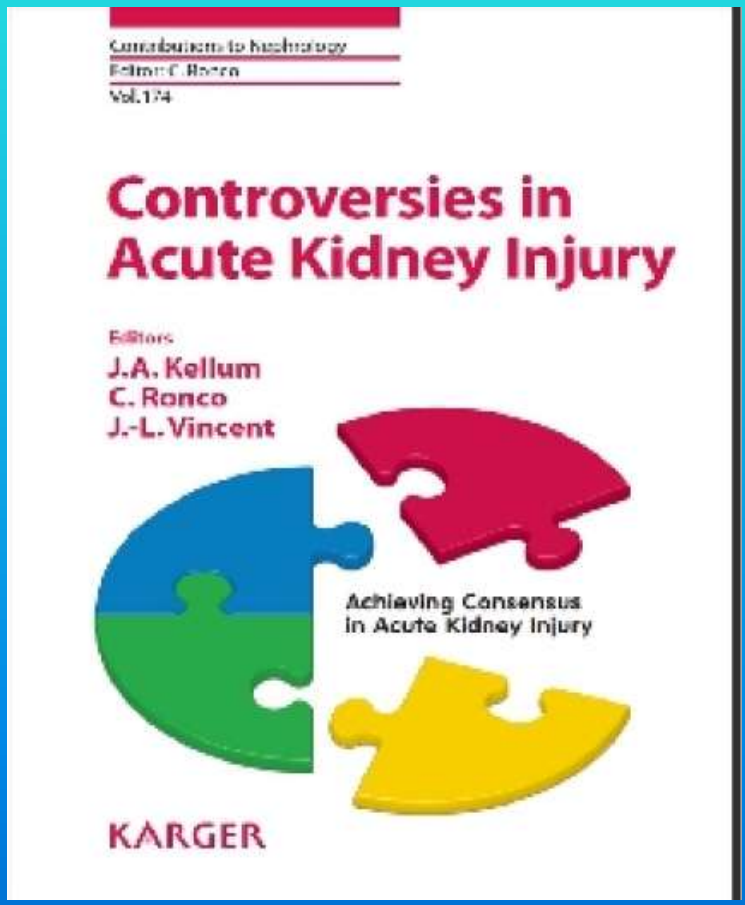

Conclusion

- **A specific RRT that could be defined "adequate" for all patients in all conditions *does not exist* but, like mechanical ventilation, renal replacement should be continuously tailored on patients' characteristics and frequently modified.**

- **In patients with AKI who are haemodynamically stable, the RRT modality does not appear to influence important patient outcomes in the light of available evidence.**

- **In haemodynamically unstable patients, CRRT may however be preferable as patients on CRRT appear to achieve higher MAP and show a trend towards lesser need for escalation of vasopressor therapy and arrhythmias.**

Definitely, this is an area of controversy



Thank you